FIG. 1

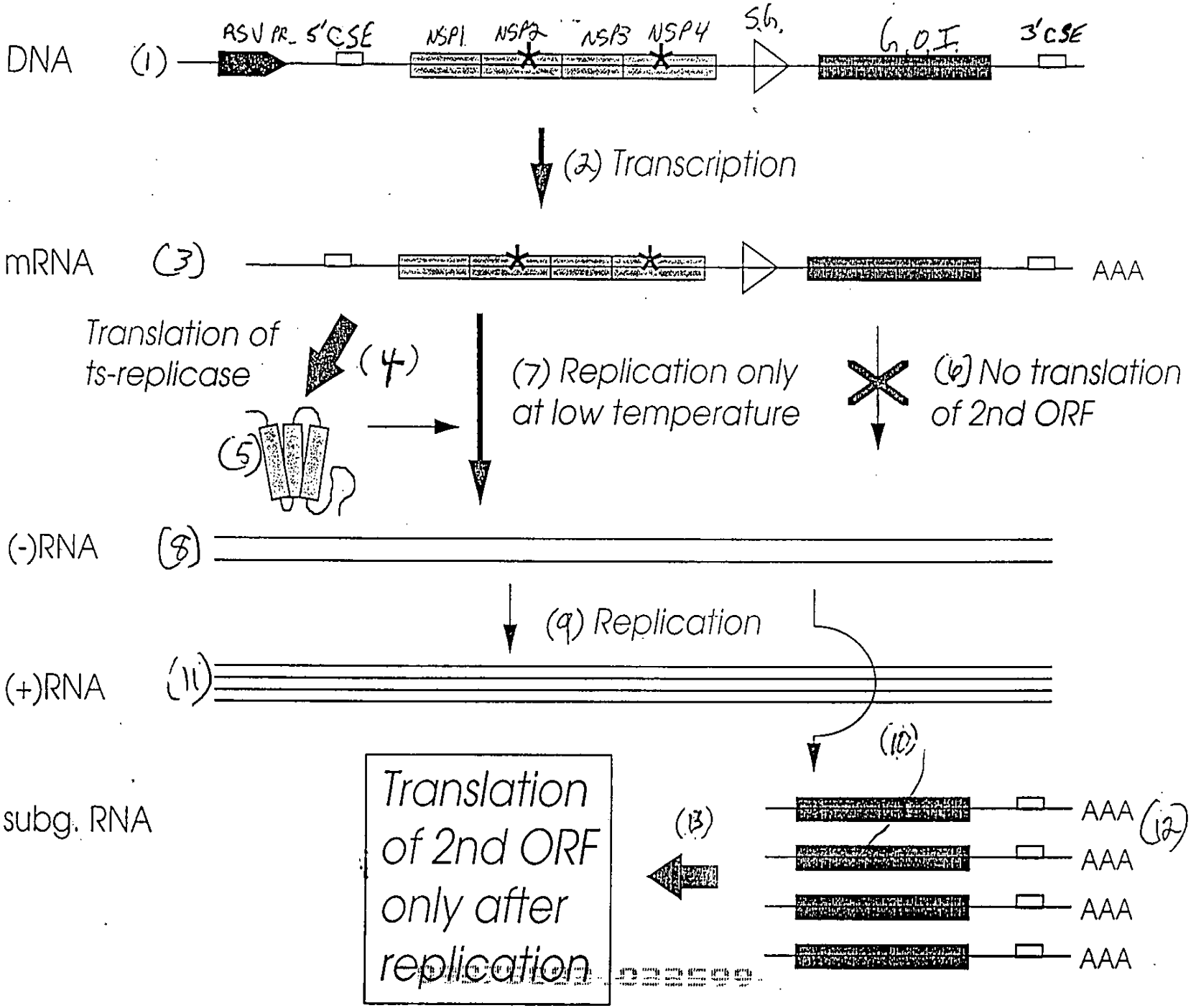
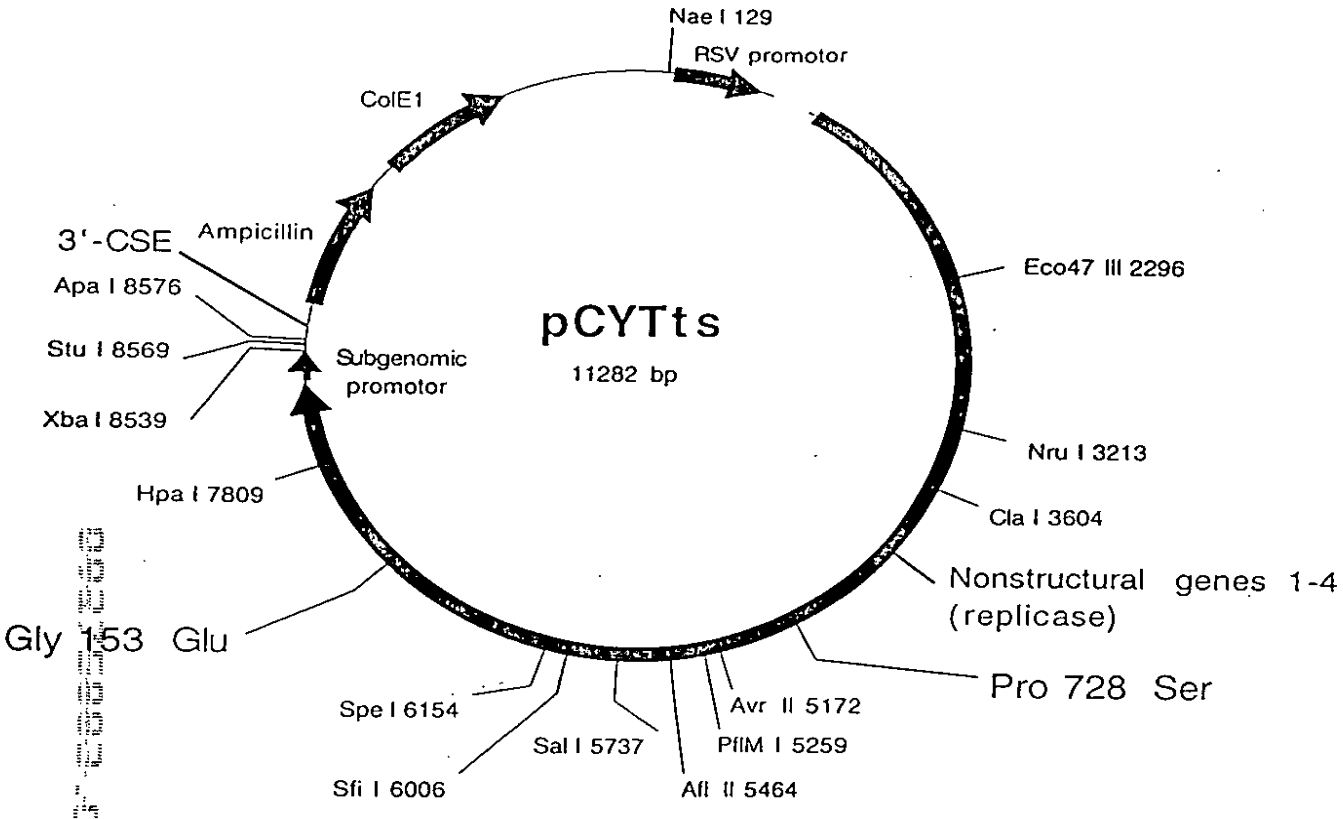

DNA
(1)
RSV PR
5'CSE
NSP1
NSP2
NSP3
NSP4
S.h.
G.O.I.
3'CSE
(2) Transcription
mRNA
(3)
AAA
Translation of ts-replicase
(4)
(5)
(7) Replication only at low temperature
(6) No translation of 2nd ORF
(-)RNA
(8)
(9) Replication
(+)RNA
(11)
(10)
subg. RNA
(12)
AAA
AAA
AAA
AAA
(13)
Translation of 2nd ORF only after replication

FIG. 2



15 05 05 05

FIG. 3A

CTGACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCC
CTAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGG
GCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGGTGATGGTTCACGTAGTG
GGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACT
GGAACAACACTCAACCCTATCTCGGTCTATTCTTTTGATTTATAAGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAA
TGAGCTGATTTAACAAAAATTTAACGCGAATTTTAACAAAATATTAACGCTTACAATTTCCATTCGCCATTCAGGCTGCG
CAACTGTTGGGAAGGGCGATCGGTGCGGGCCTCTTCGCTATTACGCCAGCTGGCGAAAGGGGGATGTGCTGCAAGGCGAT
TAAGTTGGGTAACGCCAGGGTTTTCCCAGTCACGACGTTGTAAAACGACGGCCAGTGAgcgcgcaattaaccctcactaa
agggaacaaaagctggctagtgGATCCAGTCTTATGCAATACTCTTGTAGTCTTGCAACATGGTAACGATGAGTTAGCAA
CATGCCTTACAAGGAGAGAAAAAGCACCGTGCATGCCGATTGGTGGAAGTAAGGTGGTACGATCGTGCCTTATTAGGAAG
GCAACAGACGGGTCTGACATGGATTGGACGAACCACTGAATTCCGCATTGCAGAGATATTGTATTTAAGTGCCCTACCTc
gataccgTCGAGATTGACGGCGTAGTACACACTATTGAATCAAACAGCCGACCAATTGCACTACCATCACAATGGAGAAG
CCAGTAGTAAACGTAGACGTAGACCCCCAGAGTCCGTTTGTCGTGCAACTGCAAAAAAGCTTCCCGCAATTTGAGGTAGT
AGCACAGCAGGTCACTCCAAATGACCATGCTAATGCCAGAGCATTTTCGCATCTGGCCAGTAAACTAATCGAGCTGGAGG
TTCCTACCACAGCGACGATCTTGGACATAGGCAGCGCACCGGCTCGTAGAATGTTTTCCGAGCACCAGTATCATTGTGTC
TGCCCCATGCGTAGTCCAGAAGACCCGGACCGCATGATGAAATACGCCAGTAAACTGGCGGAAAAAGCGTGCAAGATTAC
AAACAAGAACTTGCATGAGAAGATTAAGGATCTCCGGACCGTACTTGATACGCCGGATGCTGAAACACCATCGCTCTGCT
TTCACAACGATGTTACCTGCAACATGCGTGCCGAATATTCCGTCATGCAGGACGTGTATATCAACGCTCCCGGAACTATC
TATCATCAGGCTATGAAAGGCGTGCGGACCCTGTACTGGATTGGCTTCGACACCACCCAGTTCATGTTCTCGGCTATGGC
AGGTTCGTACCCTGCGTACAACACCAACTGGGCCGACGAGAAAGTCCTTGAAGCGCGTAACATCGGACTTTGCAGCACAA
AGCTGAGTGAAGGTAGGACAGGAAAATTGTCGATAATGAGGAAGAAGGAGTTGAAGCCCGGGTCGCGGGTTTATTTCTCC
GTAGGATCGACACTTTATCCAGAACACAGAGCCAGCTTGCAGAGCTGGCATCTTCCATCGGTGTTCCACTTGAATGGAAA
GCAGTCGTACACTTGCCGCTGTGATACAGTGGTGAGTTGCGAAGGCTACGTAGTGAAGAAAATCACCATCAGTCCCGGGA
TCACGGGAGAAACCGTGGGATACGCGGTTACACACAATAGCGAGGGCTTCTTGCTATGCAAAGTTACTGACACAGTAAAA
GGAGAACGGGTATCGTTCCCTGTGTGCACGTACATCCCGGCCACCATATGCGATCAGATGACTGGTATAATGGCCACGGA
TATATCACCTGACGATGCACAAAAACTTCTGGTTGGGCTCAACCAGCGAATTGTCATTAACGGTAGGACTAACAGGAACA
CCAACACCATGCAAAATTACCTTCTGCCGATCATAGCACAAGGGTTCAGCAAATGGGCTAAGGAGCGCAAGGATGATCTT
GATAACGAGAAAATGCTGGGTACTAGAGAACGCAAGCTTACGTATGGCTGCTTGTGGGCGTTTCGCACTAAGAAAGTACA
TTCGTTTTATCGCCCACCTGGAACGCAGACCTGCGTAAAAGTCCCAGCCTCTTTTAGCGCTTTTCCCATGTCGTCCGTAT
GGACGACCTCTTTGCCCATGTCGCTGAGGCAGAAATTGAAACTGGCATTGCAACCAAAGAAGGAGGAAAAACTGCTGCAG
GTCTCGGAGGAATTAGTCATGGAGGCCAAGGCTGCTTTTGAGGATGCTCAGGAGGAAGCCAGAGCGGAGAAGCTCCGAGA
AGCACTTCCACCATTAGTGGCAGACAAAGGCATCGAGGCAGCCGCAGAAGTTGTCTGCGAAGTGGAGGGGCTCCAGGCGG
ACATCGGAGCAGCATTAGTTGAAACCCCGCGCGGTCACGTAAGGATAATACCTCAAGCAAATGACCGTATGATCGGACAG
TATATCGTTGTCTCGCCAAACTCTGTGCTGAAGAATGCCAAACTCGCACCAGCGCACCCGCTAGCAGATCAGGTTAAGAT
CATAACACACTCCGGAAGATCAGGAAGGTACGCGGTCGAACCATACGACGCTAAAGTACTGATGCCAGCAGGAGGTGCCG
TACCATGGCCAGAATTCCTAGCACTGAGTGAGAGCGCCACGTTAGTGTACAACGAAAGAGAGTTTGTGAACCGCAAACTA
TACCACATTGCCATGCATGGCCCCGCCAAGAATACAGAAGAGGAGCAGTACAAGGTTACAAAGGCAGAGCTTGCAGAAAC
AGAGTACGTGTTTGACGTGGACAAGAAGCGTTGCGTTAAGAAGGAAGAAGCCTCAGGTCTGGTCCTCTCGGGAGAACTGA
CCAACCCTCCCTATCATGAGCTAGCTCTGGAGGGACTGAAGACCCGACCTGCGGTCCCGTACAAGGTCGAAACAATAGGA
GTGATAGGCACACCGGGGTCGGGCAAGTCAGCTATTATCAAGTCAACTGTCACGGCACGAGATCTTGTTACCAGCGGAAA
GAAAGAAAATTGTCGCGAAATTGAGGCCGACGTGCTAAGACTGAGGGGTATGCAGATTACGTCGAAGACAGTAGATTCGG
TTATGCTCAACGGATGCCACAAAGCCGTAGAAGTGCTGTACGTTGACGAAGCGTTCGCGTGCCACGCAGGAGCACTACTT
GCCTTGATTGCTATCGTCAGGCCCCGCAAGAAGGTAGTACTATGCGGAGACCCCATGCAATGCGGATTCTTCAACATGAT
GCAACTAAAGGTACATTTCAATCACCCTGAAAAAGACATATGCACCAAGACATTCTACAAGTATATCTCCCGGCGTTGCA

FIG. 3B

CACAGCCAGTTACAGCTATTGTATCGACACTGCATTACGATGGAAAGATGAAAACCACGAACCCGTGCAAGAAGAACATT
GAAATCGATATTACAGGGGCCACAAAGCCGAAGCCAGGGGATATCATCCTGACATGTTTCCGCGGGTGGGTTAAGCAATT
GCAAATCGACTATCCCGGACATGAAGTAATGACAGCCGCGGCCTCACAAGGGCTAACCAGAAAAGGAGTGTATGCCGTCC
GGCAAAAAGTCAATGAAAACCCACTGTACGCGATCACATCAGAGCATGTGAACGTGTTGCTCACCCGCACTGAGGACAGG
CTAGTGTGGAAAACCTTGCAGGGCGACCCATGGATTAAGCAGCCCACTAACATACCTAAAGGAAACTTTCAGGCTACTAT
AGAGGACTGGGAAGCTGAACACAAGGGAATAATTGCTGCAATAAACAGCCCCACTCCCCGTGCCAATCCGTTCAGCTGCA
AGACCAACGTTTGCTGGGCGAAAGCATTGGAACCGATACTAGCCACGGCCGGTATCGTACTTACCGGTTGCCAGTGGAGC
GAACTGTTCCCACAGTTTGCGGATGACAAACCACATTCGGCCATTTACGCCTTAGACGTAATTTGCATTAAGTTTTTCGG
CATGGACTTGACAAGCGGACTGTTTTCTAAACAGAGCATCCCACTAACGTACCATCCCGCCGATTCAGCGAGGCCGGTAG
CTCATTGGGACAACAGCCCAGGAACCCGCAAGTATGGGTACGATCACGCCATTGCCGCCGAACTCTCCCGTAGATTTCCG
GTGTTCCAGCTAGCTGGGAAGGGCACACAACTTGATTTGCAGACGGGGAGAACCAGAGTTATCTCTGCACAGCATAACCT
GGTCCCGGTGAACCGCAATCTTCCTCACGCCTTAGTCCCCGAGTACAAGGAGAAGCAACCCGGCCCGGTCAAAAAATTCT
TGAACCAGTTCAAACACCACTCAGTACTTGTGGTATCAGAGGAAAAAATTGAAGCTCCCCGTAAGAGAATCGAATGGATC
GCCCCGATTGGCATAGCCGGTGCAGATAAGAACTACAACCTGGCTTTCGGGTTTCCGCCGCAGGCACGGTACGACCTGGT
GTTCATCAACATTGGAACTAAATACAGAAACCACCACTTTCAGCAGTGCGAAGACCATGCGGCGACCTTAAAAACCCTTT
CGCGTTCGGCCCTgaattgTTtAaacTcaggaggcacCCTCGTGGTGAAGTCCTATGGCTACGCCGACCGCAACAGTGAG
GACGTAGTCACCGCTCTTGCCAGAAAGTTTGTCAGGGTGTCTGCAGCGAGACCAGATTGTGTCTCAAGCAATACAGAAAT
GTACCTGATTTTCCGACAACTAGACAACAGCCGTACACGGCAATTCACCCCGCACCATCTGAATTGCGTGATTTCGTCCG
TGTATGAGGGTACAAGAGATGGAGTTGGAGCCGCGCCGTCATACCGCACCAAAAGGGAGAATATTGCTGACTGTCAAGAG
GAAGCAGTTGTCAACGCAGCCAATCCGCTGGGTAGACCAGGCGAAGGAGTCTGCCGTGCCATCTATAAACGTTGGCCGAC
CAGTTTTACCGATTCAGCCACGGAGACAGGCACCGCAAGAATGACTGTGTGCCTAGGAAAGAAAGTGATCCACGCGGTCG
GCCCTGATTTCCGGAAGCACCCAGAAGCAGAAGCCTTGAAATTGCTACAAAACGCCTACCATGCAGTGGCAGACTTAGTA
AATGAACATAACATCAAGTCTGTCGCCATTCCACTGCTATCTACAGGCATTTACGCAGCCGGAAAAGACCGCCTTGAAGT
ATCACTTAACTGCTTGACAACCGCGCTAGACAGAACTGACGCGGACGTAACCATCTATTGCCTGGATAAGAAGTGGAAGG
AAAGAATCGACGCGGCACTCCAACTTAAGGAGTCTGTAACAGAGCTGAAGGATGAAGATATGGAGATCGACGATGAGTTA
GTATGGATtCATCCAGACAGTTGCTTGAAGGGAAGAAAGGGATTCAGTACTACAAAAGGAAAATTGTATTCGTACTTCGA
AGGCACCAAATTCCATCAAGCAGCAAAAGACATGGCGGAGATAAAGGTCCTGTTCCCTAATGACCAGGAAAGTAATGAAC
AACTGTGTGCCTACATATTGGGTGAGACCATGGAAGCAATCCGCGAAAAGTGCCCGGTCGACCATAACCCGTCGTCTAGC
CCGCCCAAAACGTTGCCGTGCCTTTGCATGTATGCCATGACGCCAGAAAGGGTCCACAGACTTAGAAGCAATAACGTCAA
AGAAGTTACAGTATGCTCCTCCACCCCCCTTCCTAAGCACAAAATTAAGAATGTTCAGAAGGTTCAGTGCACGAAAGTAG
TCCTGTTTAATCCGCACACTCCCGCATTCGTTCCCGCCCGTAAGTACATAGAAGTGCCAGAACAGCCTACCGCTCCTCCT
GCACAGGCCGAGGAGGCCCCCGAAGTTGTAGCGACACCGTCACCATCTACAGCTGATAACACCTCGCTTGATGTCACAGA
CATCTCACTGGATATGGATGACAGTAGCGAAGGCTCACTTTTTTCGAGCTTTAGCGGATCGGACAACTCTATTACTAGTA
TGGACAGTTGGTCGTCAGGACCTAGTTCACTAGAGATAGTAGACCGAAGGCAGGTGGTGGTGGCTGACGTTCATGCCGTC
CAAGAGCCTGCCCCTATTCCACCGCCAAGGCTAAAGAAGATGGCCCGCCTGGCAGCGGCAAGAAAAGAGCCCACTCCACC
GGCAAGCAATAGCTCTGAGTCCCTCCACCTCTCTTTTGGTGGGGTATCCATGTCCCTCGGATCAATTTTCGACGGAGAGA
CGGCCCGCCAGGCAGCGGTACAACCCCTGGCAACAGGCCCCACGGATGTGCCTATGTCTTTCGGATCGTTTTCCGACGGA
GAGATTGATGAGCTGAGCCGCAGAGTAACTGAGTCCGAACCCGTCCTGTTTGGATCATTTGAACCGGGCGAAGTGAACTC
AATTATATCGTCCCGATCAGCCGTATCTTTTCCACTACGCAAGCAGAGACGTAGACGCAGGAGCAGGAGGACTGAATACT
GACTAACCGGGGTAGGTGGGTACATATTTTCGACGGACACAGGCCCTGGGCACTTGCAAAAGAAGTCCGTTCTGCAGAAC
CAGCTTACAGAACCGACCTTGGAGCGCAATGTCCTGGAAAGAATTCATGCCCCGGTGCTCGACACGTCGAAAGAGGAACA
ACTCAAACTCAGGTACCAGATGATGCCCACCGAAGCCAACAAAAGTAGGTACCAGTCTCGTAAAGTAGAAAATCAGAAAG
CCATAACCACTGAGCGACTACTGTCAGGACTACGACTGTATAACTCTGCCACAGATCAGCCAGAATGCTATAAGATCACC
TATCCGAAACCATTGTACTCCAGTAGCGTACCGGCGAACTACTCCGATCCACAGTTCGCTGTAGCTGTCTGTAACAACTA

FIG. 3C

TCTGCATGAGAACTATCCGACAGTAGCATCTTATCAGATTACTGACGAGTACGATGCTTACTTGGATATGGTAGACGaGA
CAGTCGCaTGCCTGGATACTGCAACCTTCTGCCCCGCTAAGCTTAGAAGTTACCCGAAAAAACATGAGTATAGAGCCCCG
AATATCCGCAGTGCGGTTCCATCAGCGATGCAGAACACGCTACAAAATGTGCTCATTGCCGCAACTAAAAGAAATTGCAA
CGTCACGCAGATGCGTGAACTGCCAACACTGGACTCAGCGACATTCAATGTCGAATGCTTTCGAAAATATGCATGTAATG
ACGAGTATTGGGAGGAGTTCGCTCGGAAGCCAATTAGGATTACCACTGAGTTTGTCACCGCATATGTAGCTAGACTGAAA
GGCCCTAAGGCCGCCGCACTATTTGCAAAGACGTATAATTTGGTCCCATTGCAAGAAGTGCCTATGGATAGATTCGTCAT
GGACATGAAAAGAGACGTGAAAGTTACACCAGGCACGAAACACACAGAAGAAAGACCGAAAGTACAAGTGATACAAGCCG
CAGAACCCCTGGCGACTGCTTACTTATGCGGGATTCACCGGGAATTAGTGCGTAGGCTTACGGCCGTCTTGCTTCCAAAC
ATTCACACGCTTTTTGACATGTCGGCGGAGGATTTTGATGCAATCATAGCAGAACACTTCAAGCAAGGCGACCCGGTACT
GGAGACGGATATCGCATCATTCGACAAAAGCCAAGACGACGCTATGGCGTTAACCGGTCTGATGATCTTGGAGGACCTGG
GTGTGGATCAACCACTACTCGACTTGATCGAGTGCGCCTTTGGAGAAATATCATCCACCCATCTACCTACGGGTACTCGT
TTTAAATTCGGGGCGATGATGAAATCCGGAATGTTCCTCACACTTTTTGTCAACACAGTTTTGAATGTCGTTATCGCCAG
CAGAGTACTAGAAGAGCGGCTTAAAACGTCCAGATGTGCAGCGTTCATTGGCGACGACAACATCATACATGGAGTAGTAT
CTGACAAAGAAATGGCTGAGAGGTGCGCCACCTGGCTCAACATGGAGGTTAAGATCATCGACGCAGTCATCGGTGAGAGA
CCACCTTACTTCTGCGGCGGATTTATCTTGCAAGATTCGGTTACTTCCACAGCGTGCCGCGTGGCGGATCCCCTGAAAAG
GCTGTTTAAGTTGGGTAAACCGCTCCCAGCCGACGACGAGCAAGACGAAGACAGAAGACGCGCTCTGCTAGATGAAACAA
AGGCGTGGTTTAGAGTAGGTATAACAGGCACTTTAGCAGTGGCCGTGACGACCCGGTATGAGGTAGACAATATTACACCT
GTCCTACTGGCATTGAGAACTTTTGCCCAGAGCAAAAGAGCATTCCAAGCCATCAGAGGGGAAATAAAGCATCTCTACGG
TGGTCCTAAATAGTCAGCATAGTACATTTCATCTGACTAATACTACAACACCACCACCtctagaCGCGTAGAtctcacgt
gagcatgcaggccttgggCCCAATGATCCGACCAGCAAAACTCGATGTACTTCCGAGGAACTGATGTGCATAATGCATCA
GGCTGGTACATTAGATCCCCGCTTACCGCGGGCAATATAGCAACACTAAAAACTCGATGTACTTCCGAGGAAGCGCAGTG
CATAATGCTGCGCAGTGTTGCCACATAACCACTATATTAACCATTTATCTAGCGGACGCCAAAAACTCAATGTATTTCTG
AGGAAGCGTGGTGCATAATGCCACGCAGCGTCTGCATAACTTTTATTATTTCTTTTATTAATCAACAAAATTTTGTTTTT
AACATTTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGGGAATTCCCAACTTGTTTATTGCAGCTTATAATG
GTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAA
CTCATCAATGTATCTTATCATGTCTGGATCCGTCGAGACGCGTccaattcgccctatagtgagtcgtattacgcgcgcTT
GGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCA
TAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCG
GGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGC
TTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGT
TATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCC
GCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAA
CCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTA
CCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTG
TAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCG
TCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATG
TAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTG
CTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTT
TGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTC
AGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAA
AAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACC
TATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCT
TACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCA
GCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAG

FIG. 3D

AGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTG
GTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGC
TCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTC
TCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGC
GGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATT
GGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACC
CAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGG
GAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGT
CTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCC
AC

10/550,477 - 10 - 10/550,477

FIG. 4A

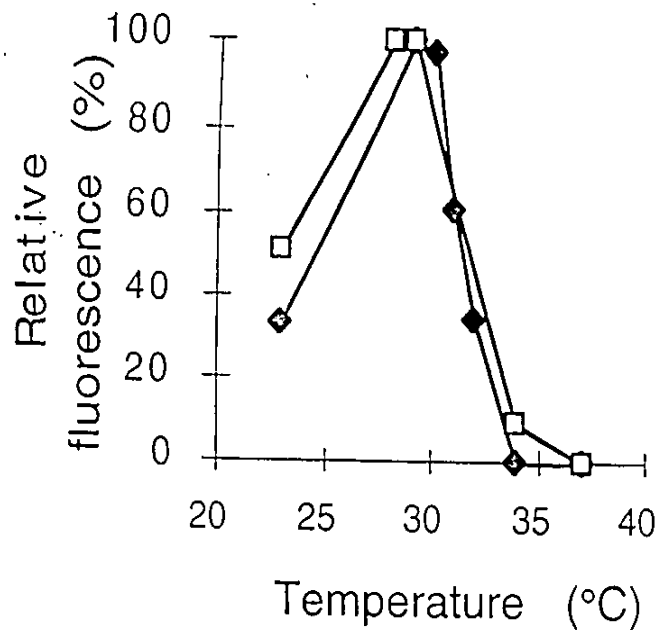

Relative fluorescence (%)
100
80
60
40
20
0
20
25
30
35
40
Temperature (°C)

FIG. 4B

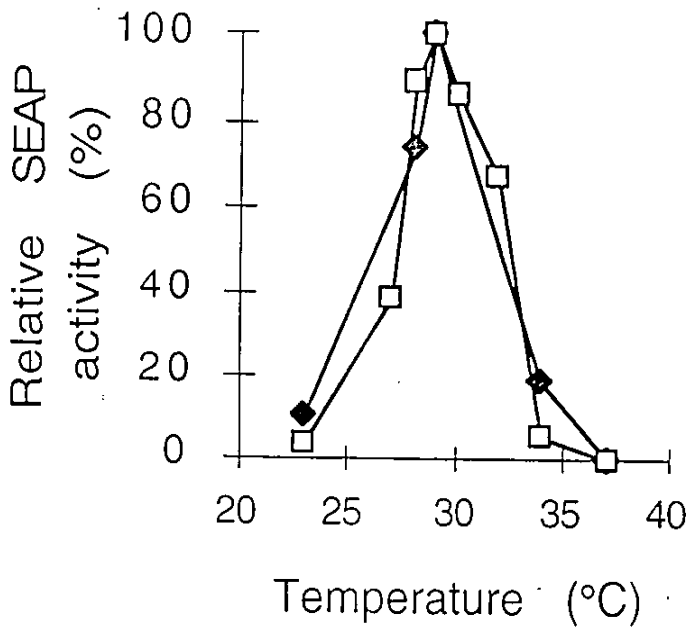

Relative SEAP activity (%)
100
80
60
40
20
0
20
25
30
35
40
Temperature (°C)

FIG. 5A

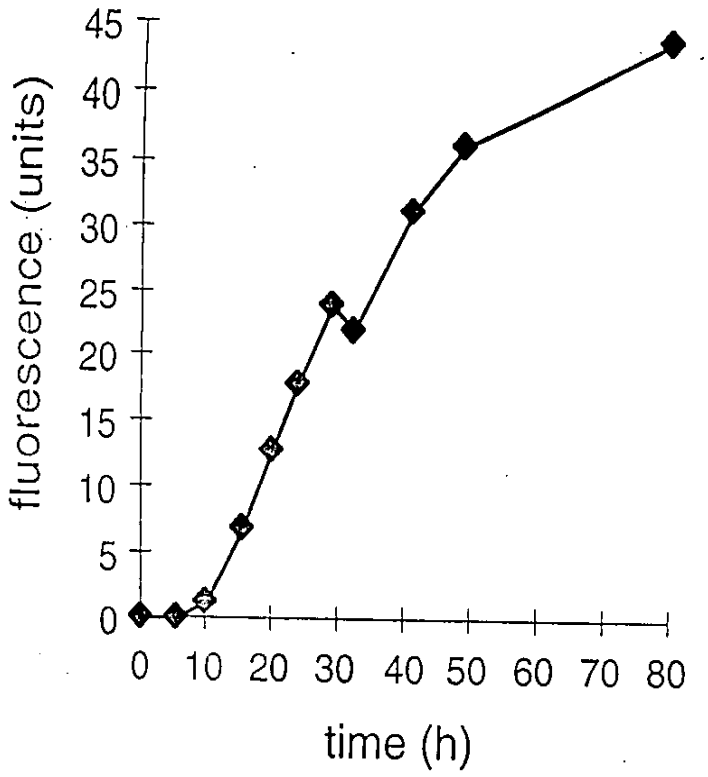

fluorescence (units)
45
40
35
30
25
20
15
10
5
0
0 10 20 30 40 50 60 70 80
time (h)

FIG. 5B

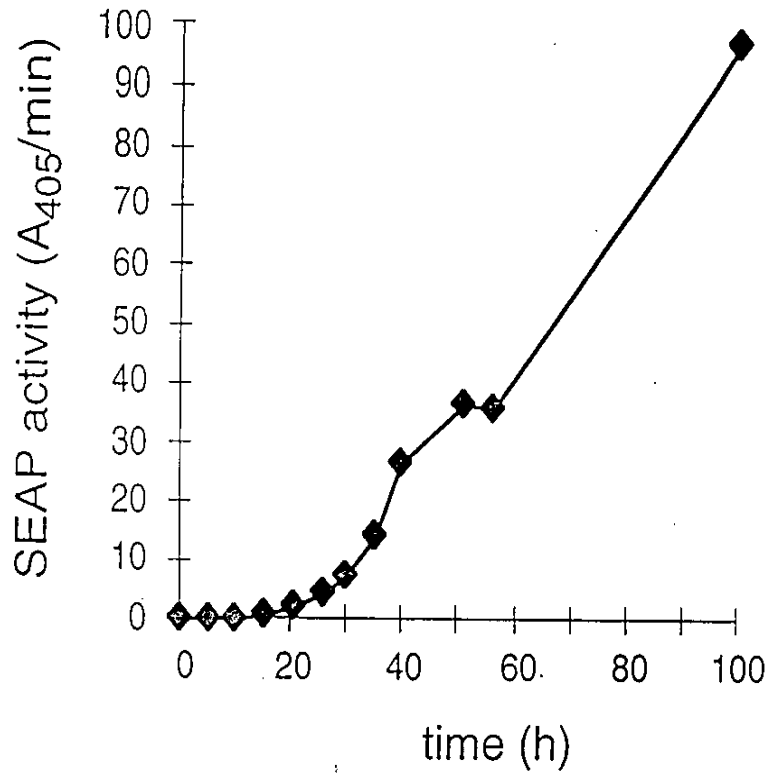

SEAP activity (A_{405}/min)
100
90
80
70
60
50
40
30
20
10
0
0 20 40 60 80 100
time (h)

FIG. 6A

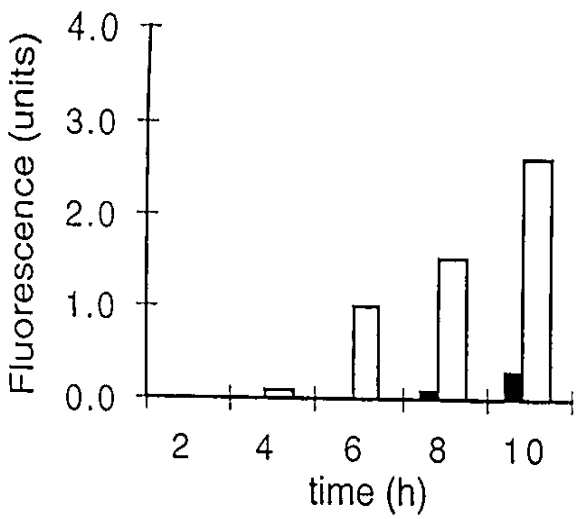

Fluorescence (units)
4.0
3.0
2.0
1.0
0.0
2
4
6
8
10
time (h)

FIG. 6B

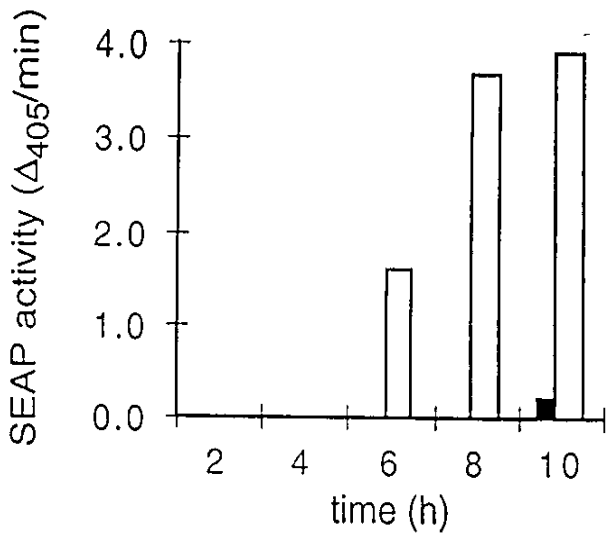

SEAP activity (Δ_{405}/min)
4.0
3.0
2.0
1.0
0.0
2
4
6
8
10
time (h)

FIG. 7A

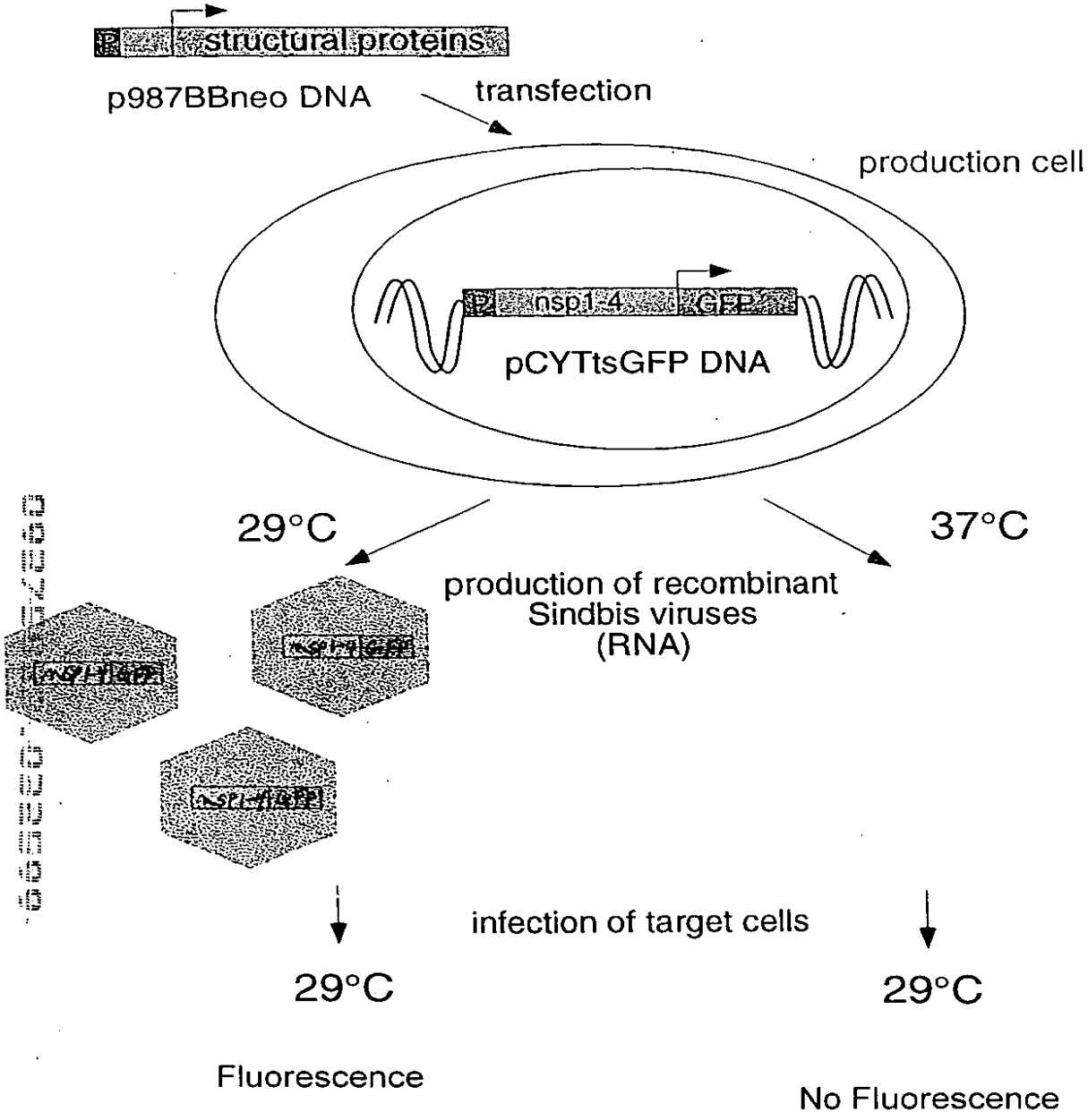

P
structural proteins
p987BBneo DNA
transfection
production cell
P
nsp1-4
GFP
pCYTtsGFP DNA
29°C
37°C
production of recombinant
Sindbis viruses
(RNA)
infection of target cells
29°C
29°C
Fluorescence
No Fluorescence

FIG. 7B

FIG. 8A

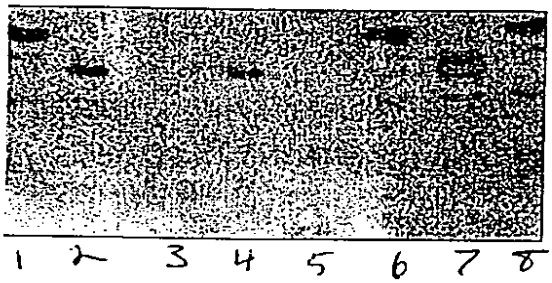


FIG. 8B

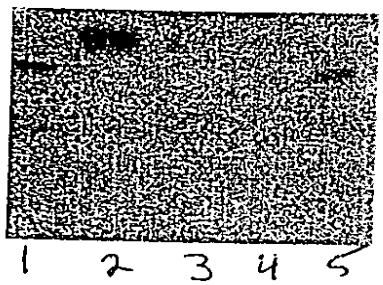
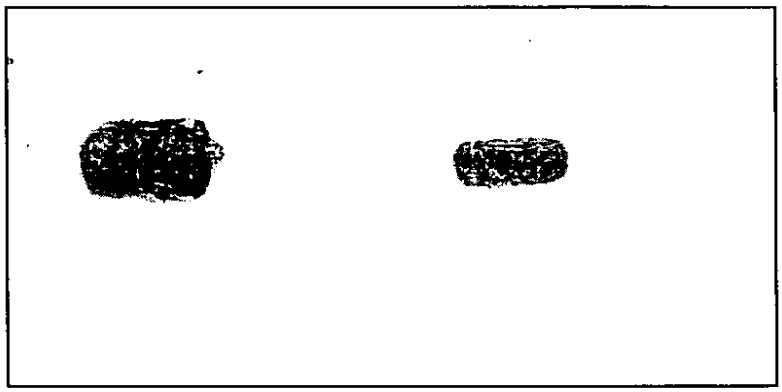


Fig. 9



1 2 3 4

Fig. 10

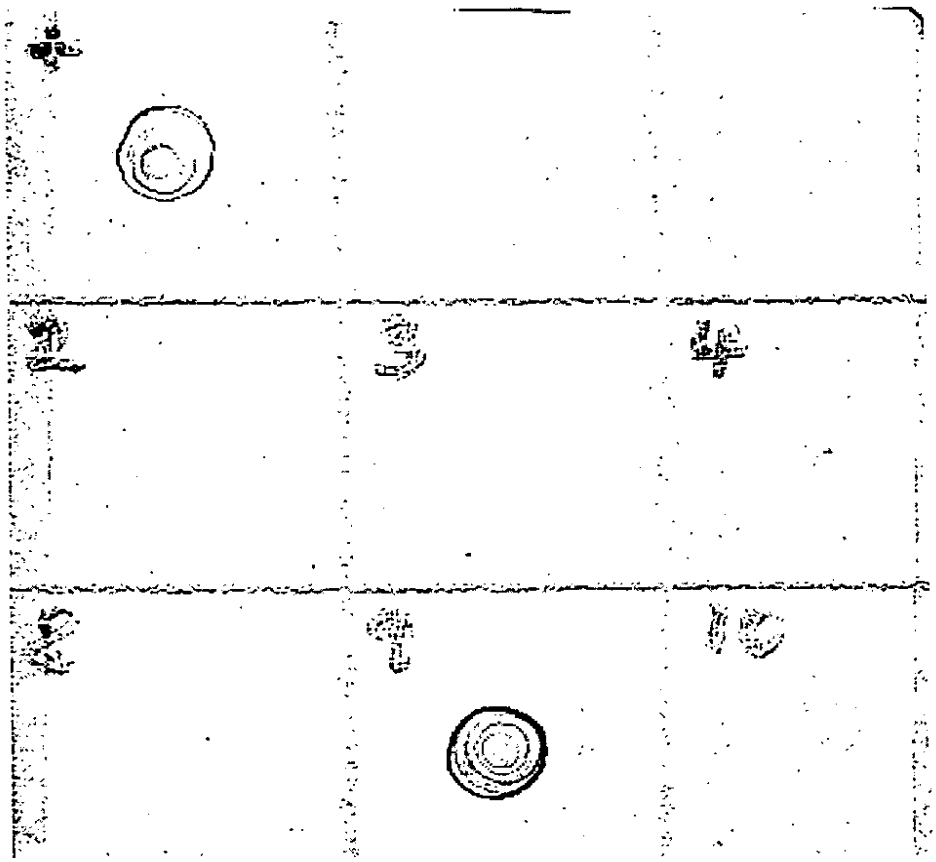


FIG. 11

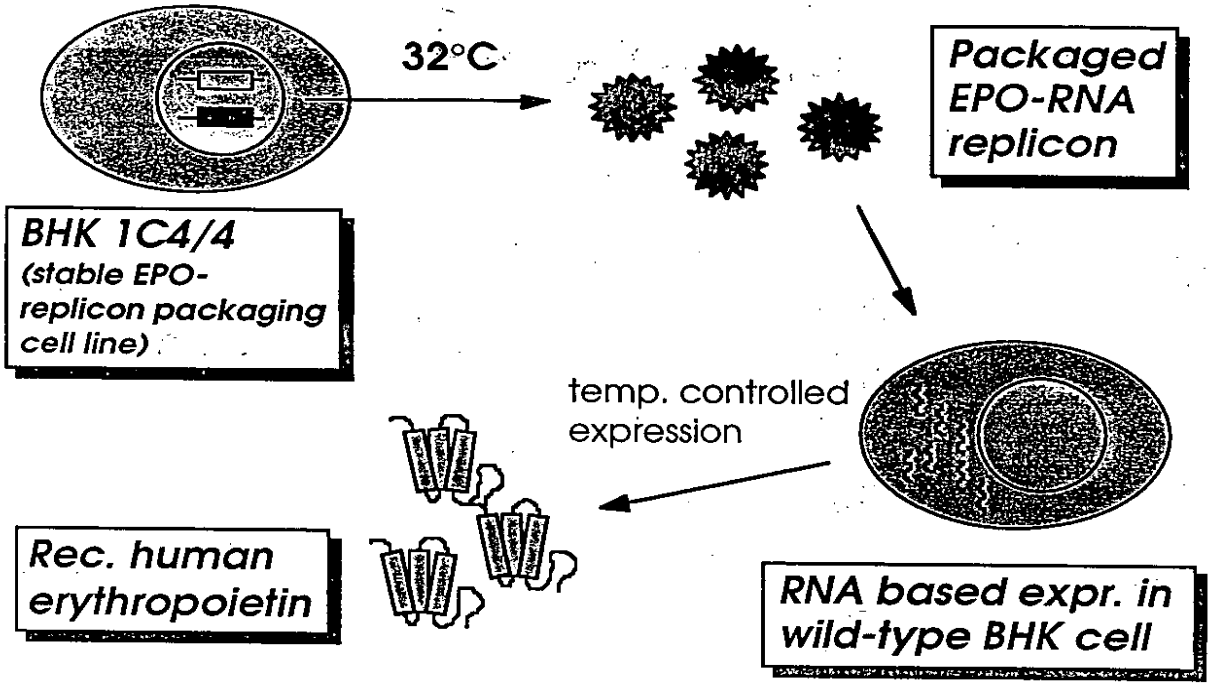
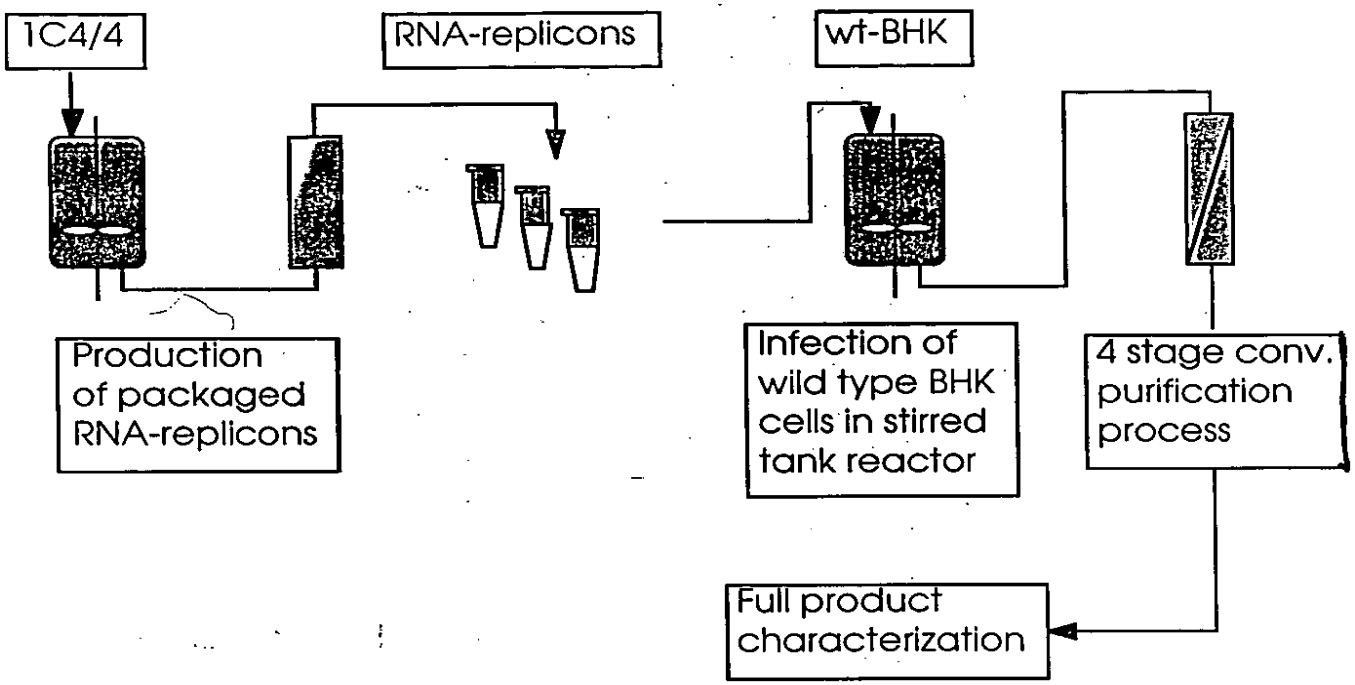

32°C
Packaged EPO-RNA replicon
BHK 1C4/4 (stable EPO-replicon packaging cell line)
temp. controlled expression
Rec. human erythropoietin
RNA based expr. in wild-type BHK cell

FIG. 12


1C4/4
RNA-replicons
wt-BHK
Production of packaged RNA-replicons
Infection of wild type BHK cells in stirred tank reactor
4 stage conv. purification process
Full product characterization